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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/606,369	06/28/2000	John R. Stuelpnagel	A-67493-3/DJB/RMS/DCF	6020
29389	7590	04/21/2005	EXAMINER	
ILLUMINA, INC. 9885 TOWNE CENTRE DRIVE SAN DIEGO, CA 92121-1975			BEISNER, WILLIAM H	
			ART UNIT	PAPER NUMBER
			1744	
DATE MAILED: 04/21/2005				

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/606,369

Applicant(s)

STUELPNAGEL ET AL.

Examiner

William H. Beisner

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11/23/04;1/21/05;3/7/05.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 29-52 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 29-52 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>1/21/05 & 3/7/05</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/23/2004 has been entered.

Information Disclosure Statement

2. The information disclosure statements filed 1/21/2005 and 3/7/2005 have been considered and made of record.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

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4. Considering objective evidence present in the application indicating obviousness or nonobviousness.
5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).
6. Claims 29-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Whitehead et al.(US 4,879,097) in view of Kolehmainen et al.(US 4,349,510) and Tajima et al.(US 5,682,232).

The reference of Whitehead et al. discloses a device for forming a chamber which includes a base plate (10, 11) which holds a microtiter plate (16, 17). The device includes a lid including component ports for immobilizing array components (28 or 350). The device includes sealant (21) between the base and the lid.

While the reference of Whitehead et al. discloses sealant, 21, so as to seal the chamber to prevent entry of stray light (See the abstract), the instant claims recite that the sealant provides an "airtight" seal.

The reference of Kolehmainen et al. discloses an optical analysis system which detects chemiluminescence. The reference of Kolehmainen et al. discloses that a light-tight seal can be

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maintained using an o-ring, 38 (See column 4, lines 6-27). The light-tight seal prevents external light from interfering with the detector.

In view of this teaching and in the absence of a showing of criticality and/or unexpected results, it would have been obvious to one of ordinary skill in the art to employ an o-ring seal in place of seal, 21, in device of Whitehead et al. for the known and expected result of providing an alternative means recognized in the art to achieve the same result, sealing the interior of the reaction region from exterior light. Use of an o-ring as suggested by the reference of Kolehmainen et al. would inherently result in an airtight seal. Furthermore, the use of an o-ring to form the light-tight seal of Whitehead et al. would be advantageous over the seal (21) of Whitehead et al. because the o-ring would also provide an air-tight seal that would provide better contamination protection with respect to contaminants entering the reaction chamber.

While the combination of the references of Whitehead et al. and Kolehmainen et al. suggests the use of an o-ring-type of seal for creating a light-tight seal, the instant claims further differ by reciting that the device includes “a clamp providing increased pressure between said lid and said base plate”.

The reference of Tajima et al. discloses that when forming a light-tight seal between a base plate (9) and a lid (5) it is known in the art to employ an elastic sealing member (See column 4, lines 43-53). The reference also discloses the use of a clamping device (8) for increasing the pressure between the lid (5) and the base plate (9).

In view of this teaching, it would have been obvious to one of ordinary skill in the art at the time the invention was made to provide the device of the modified primary reference with a clamp device for the known and expected result of providing an art recognized means for

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comprising an elastic sealing member, such as an o-ring, so as to provide a light-tight seal with respect to the lid and base plate of the detection housing.

With respect to claim 29, the lid of the device of Whitehead et al. includes openings or ports that include second array components (28, 129, 228).

With respect to claim 30, the first array component is a microtiter plate (16,17).

With respect to claim 31, the references of Whitehead et al. and Kolehmainen et al. discloses that is it known in the art to monitor chemiluminescent or bioluminescent reactions performed in microtiter plate arrays using an array of fiber optic devices (See Column 4, lines 61-66 of Whitehead et al. and Figure 4 of Kolehmainen et al.).

In view of these teachings and in the absence of a showing of criticality and/or unexpected results, it would have been obvious to one of ordinary skill in the art at the time the invention was made to employ a fiber optic array in the lid structure of the reference of Whitehead et al. for the known and expected result of providing an alternative means recognized in the art to detect chemiluminescent reactions. Provision of the fiber optic and electrical detection system would provide increased reliability over the use of photographic film which is analyzed visually and/or provide an additional analytical techniques simultaneously.

With respect to claims 32 and 33, the device includes male/female alignment means (22).

With respect to claims 34 and 35, as shown in Figure 11, the chamber is connected to at least one fluid-handling device (350).

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7. Claims 36-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Whitehead et al.(US 4,879,097) in view of Kolehmainen et al.(US 4,349,510) and Tajima et al.(US 5,682,232) taken further in view of Walt et al.(US 6,327,410).

The combination of the references of Whitehead et al., Kolehmainen et al. and Tajima et al.(US 5,682,232) has been discussed above.

With respect to claims 36-40, the above claims differ by reciting that the second array component of the lid includes arrays of bioactive agents, specifically, a substrate that includes discrete sites containing a microspheres of distinctive bioactive agents.

The reference of Whitehead et al. discloses that the disclosed supports (129) can take the form of fiber optic sensors (See column 9, lines 61-66).

The reference of Walt et al. discloses that the use of a substrate including discrete sites and a population of microspheres comprising first and second subpopulations distributed on the discrete sites wherein each subpopulation includes a distinct bioactive agent is known in the art (See column 4, line 35, to column 5, line 31).

In view of this teaching, it would have been obvious to one of ordinary skill in the art to employ the fiber optic sensor devices disclosed in the reference of Walt et al. in the system of the reference of Whitehead et al. for the known and expected result of providing a means recognized in the art for contacting a fiber optic sensor with a sample for analyte detection. Advantages of using the fiber optic sensor of Walt et al. over other prior art sensors include the ease of manufacture and the ability to perform high density screening of samples. Use of the system of Whitehead et al. for contacting the fiber optic sensor with a sample of analyte would allow a

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plurality of samples to be simultaneously contacted with a plurality of separate fiber optic sensors while maintaining a light-tight environment.

With respect to claim 41, it would have been obvious to one of ordinary skill in the art to coat each support (129) with a different bioactive agent for the known and expected result of providing a means for simultaneously performing a plurality of different luminescent immunospecific assays.

With respect to claims 42 and 43, the reference of Walt et al. discloses the claimed density of bioactive agents (See column 5, lines 4-23).

With respect to claims 44 and 45, while the reference of Whitehead et al. employs a 6x10 array of wells, it would have been obvious to one of ordinary skill in the art to modify the system to employ any of the standard microplate formats known in the art.

With respect to claims 46 and 47, the device includes male/female alignment means (22).

With respect to claim 48, as shown in Figure 11, the chamber is connected to at least one fluid-handling device (350).

With respect to claims 36, 49 and 50, the reference of Walt et al. discloses the use of subpopulations and/or random array of microspheres.

With respect to claim 51, the reference of Walt et al. discloses list of possible bioactive agents (See column 7, line 55, to column 8, line 67) that includes peptides and nucleic acids.

8. Claim 52/29 is rejected under 35 U.S.C. 103(a) as being unpatentable over Whitehead et al.(US 4,879,097) in view of Kolehmainen et al.(US 4,349,510) and Tajima et al.(US 5,682,232) taken further in view of Heffelfinger et al.(US 5,784,152).

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The combination of the references of Whitehead et al., Kolehmainen et al. and Tajima et al.(US 5,682,232) has been discussed above.

Claim 52 differs by reciting that the device further includes a heating device.

The reference of Heffelfinger et al. discloses that it is conventional in the art to provide a system for optically monitoring chemical reactions within a microplate with a temperature controlled incubator (102).

In view of this teaching, it would have been obvious to one of ordinary skill in the art at the time the invention was made to provide the system of the modified primary reference with a device for controlling the temperature during the reaction for the known and expected result of ensuring that the proper temperature is maintained during the optical monitoring of the reaction. Note the temperature control device would inherently include a heating device. The temperature maintained within the device would have been merely based on the specifics of the reaction that is to be monitored within the device.

9. Claims 52/37,38,39 or 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Whitehead et al.(US 4,879,097) in view of Kolehmainen et al.(US 4,349,510), Tajima et al.(US 5,682,232) and Walt et al.(US 6,327,410) taken further in view of Heffelfinger et al.(US 5,784,152).

The combination of the references of Whitehead et al., Kolehmainen et al. Tajima et al. and Walt et al. has been discussed above.

Claim 52 differs by reciting that the device further includes a heating device.

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The reference of Heffelfinger et al. discloses that it is conventional in the art to provide a system for optically monitoring chemical reactions within a microplate with a temperature controlled incubator (102).

In view of this teaching, it would have been obvious to one of ordinary skill in the art at the time the invention was made to provide the system of the modified primary reference with a device for controlling the temperature during the reaction for the known and expected result of ensuring that the proper temperature is maintained during the optical monitoring of the reaction. Note the temperature control device would inherently include a heating device. The temperature maintained within the device would have been merely based on the specifics of the reaction that is to be monitored within the device.

Response to Arguments

10. Applicant's arguments filed 11/23/2004, see pages 9-10, have been fully considered but they are not persuasive.

With respect to the rejection of the claims over the combination of the references of Whitehead et al. (US 4,879,097) and Kolehmainen et al. (US 4,349,510), Applicants take the position that the combination of the references is improper for the following reasons:

The substitution of an o-ring for the labyrinth joint of the reference of Whitehead et al. is not a functional equivalent because "In addition to providing a light-tight seal, the labyrinth joint provides a means for aligning or registering the lid 24 with the base 10, of Whitehead."

Applicants point to column 5, lines 40-47, of the reference of Whitehead and take the position that the labyrinth seal also provides the function of alignment and registration of the tube and

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wells of the device. Applicants argue that the use of an o-ring would not provide the desired functions of the labyrinth seal of the reference of Whitehead.

In response, Applicants' comment are not found to be persuasive because Applicants' are silent as to the presence of "spigot 34" and "bores 22" which provide the required alignment and registration of the tubes and wells. The reference discloses that the groove 35 and rib 21 provide a labyrinth joint which is disclosed as functioning to provide a light-tight seal. The modification of the device of Whitehead as suggested by the prior art of record would encompass a device that replaces the labyrinth seal with an o-ring seal. The modified device would still include the alignment spigot and bores disclosed by the reference of Whitehead. As a result, even in the absence of the disclosed labyrinth seal, the lid and base would still include the required structures for alignment and registration of the tubes and wells. The Examiner would also like to point out that an amount of "play" exists between groove 35 and rib 21 that would result in some lateral movement between the lid and base (See Figures 1 and 2). Note, if the labyrinth seal provided the alignment and registration argued by applicants, the device would not require the spigots and bores.

Applicants further argue that the combination is improper because the Examiner has failed to provide adequate motivation for the combination of the references. Applicants stress that the light proof barrier (21) of Whitehead et al. is to prevent entry of light into the chamber and the purpose of the o-ring of Kolehmainen et al. is to prevent detection of outside light by separate detectors contacting the reflective tape. Applicants stress that the o-ring of Kolehmainen et al. is placed between the sample and the detector such that the detector does not detect stray, contaminating light from an adjacent well. As a result, Applicants conclude, at best, the

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reference of Kolehmainen et al. would suggest placing the o-ring between the sample well and the detector of Whitehead et al. In other word, that one of ordinary skill in the art would have been motivated to place the o-ring under the sample well of Whitehead et al. or some other way between the sample well and the film, but would not have been motivated to place a sealant between the base plate and the lid forming an airtight seal.

In response to applicant's argument above, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). In this case, the primary reference of Whitehead et al. clearly discloses the use of a light-tight seal (21) so as to prevent entry of stray light between the holder (10) and cover (24). The seal employed by Whitehead et al. is characterized as a labyrinth joint (See column 5, lines 42-43). In summary, the reference of Whitehead et al. clearly discloses the use of a "light-tight seal" between the cover (24) and the base (10). The reference of Kolehmainen et al. discloses that o-ring structure (15) is an art recognized means for making a "light-tight seal" between measuring heat (43) and well (5). In view of this disclosure, one of ordinary skill in the art would recognize that the o-ring structure of Kolehmainen et al. can be substituted for the labyrinth joint of Whitehead et al. As discussed in the M.P.E.P. at section 2144.06, substituting equivalents known for the same purpose is proper when the equivalency is recognized in the prior art. Also note "An express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious" (See *In re Fout*, 213 USPQ 532

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(CCPA 1982)). In this case, one of ordinary skill in the art when presented with the prior art references discussed above would have clearly recognized that an o-ring could be used in place of a labyrinth joint for maintaining a "light-tight seal".

With respect to the combination of the references of Whitehead et al. and Kolehmainen et al., Applicants argue that the combination of the references is improper because the Examiner has failed to point to anything specific in the cited references that would suggest the motivation to combine the reference of Whitehead with the secondary reference of Kolehmainen et al. Applicants take the position that the Examiner has merely made a "common sense" argument which is impermissible.

In response, Applicants' comments are not found to be persuasive because the Examiner is of the position that the substitution of known equivalents known for the same purpose meets the requirements set forth in 35 USC 103. The prior art of record establishes that both photographic film and fiber optic detectors are known detection systems in the art of chemiluminescent detection. Note an express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious (See *In re Fout*, 213 USPQ 532 (CCPA 1982)).

Applicants further argue that there is no teaching or suggestion in the cited references that simply replacing the labyrinth seal with an o-ring would result in an airtight seal. Applicants stress that there is no teaching or suggestion in the art of record of how to modify the device of Whitehead to form an airtight seal with an o-ring.

In response, the Examiner is of the position that the prior art of record clearly provides motivation for substituting the labyrinth seal of the Whitehead reference with an o-ring seal

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suggested in the Kolehmainen et al. reference for reasons already discussed at length above. One of ordinary skill in the art would recognize that when using an o-ring to create a light-tight seal, the o-ring would inherently be capable of providing a liquid or air-tight seal. *Merriam-Webster's Collegiate Dictionary, Tenth Edition*, defines an o-ring as “a ring (as of synthetic rubber) used as a gasket”. The dictionary defines a gasket as “a material (as rubber) or a member (as an o-ring) used to make a joint fluid tight”. In view of these facts, the Examiner is of the position that one of ordinary skill in the art would have clearly recognized how to modify the device of Whitehead et al. to include an o-ring and would have clearly recognized that the o-ring would provide a fluid-tight seal while functioning to provide the required light-tight seal of the primary reference.

With respect to the rejection of the claims over the combination of the references of Whitehead et al., Kolehmainen et al. and Walt et al., Applicants first argue that the reference of Walt et al. fails to add anything to the deficiencies associated with the combination of the references of Whitehead et al. and Kolehmainen et al. and discussed at length above. Specifically, Applicants stress that the reference of Walt et al. fails to provide motivation for replacing a labyrinth seal with an o-ring.

In response, the reference of Walt et al. was not relied upon to provide motivation for replacing a labyrinth seal with an o-ring. The combination of the references of Whitehead et al. and Kolehmainen et al. address this claim limitation. The reference of Walt et al. was relied upon as an additional teaching that addresses the obviousness of employing a second array component wherein each second array component includes “a plurality of different bioactive agents”.

With respect to the combination of the references of Whitehead et al., Kolehmainen et al. and Walt et al., Applicants further argue that the combination of the references is improper because neither the references of Whitehead et al. nor Kolehmainen et al. teach or suggest that the plurality of array components comprise an array comprising a plurality of different bioactive agents directly coupled to the second array component.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In this case, the reference of Walt et al. is relied upon as a prior art teaching as to the obviousness of employing an array component with an array of a plurality of different bioactive agents directly coupled to the second array component.

Applicants further argue that while the reference of Walt et al. discloses a plurality of different bioactive agents, the bioactive agents are attached to microspheres and are not directly attached to the second array component.

Applicants' comments are not persuasive because the microspheres with the bioactive agents attached to the fiber optic bundle meets the instant claim language. The fiber optic bundle and the microspheres make-up the second array component and the bioactive agents are directly attached to the microspheres. The Examiner's position is further supported by the instant disclosure since claim 49, which is encompassed by the language of claims 37, 38, 39 and 40, includes the use of microspheres for providing "an array comprising a plurality of different bioactive agents directly coupled to said second array component".

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With respect to the newly recited claim limitation of "a clamp", the Examiner is of the position that this newly recited claim limitation does not patentably define the instant claims over the prior art of record for the reasons set forth in the new grounds of rejection including the reference of Tajima et al.(US 5,682,232).

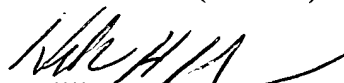
For these reasons the claims remain rejected over the prior art of record.

Conclusion

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to William H. Beisner whose telephone number is 571-272-1269. The examiner can normally be reached on Tues. to Fri. and alt. Mon. from 6:15am to 3:45pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John Kim can be reached on 571-272-1142. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


William H. Beisner
Primary Examiner
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WHB

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